# Management of Non-Melanoma Skin Cancers

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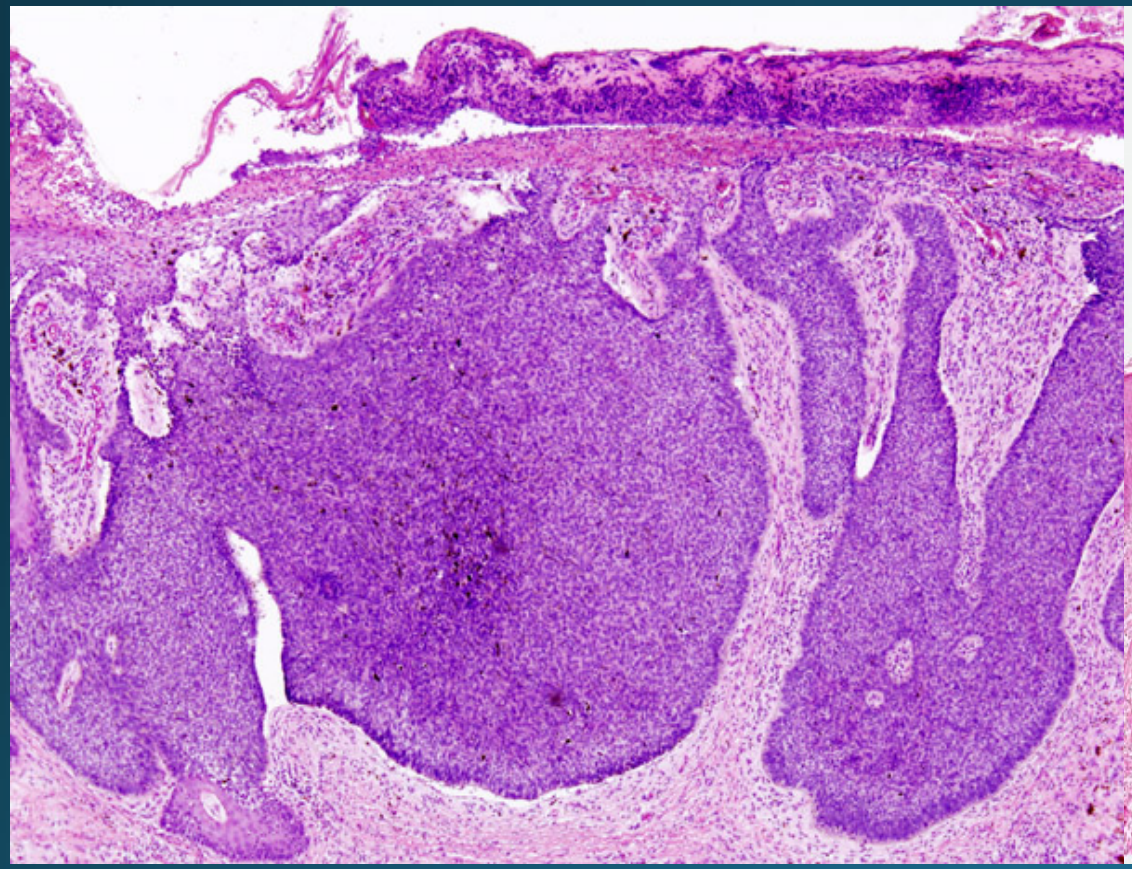
# Outline

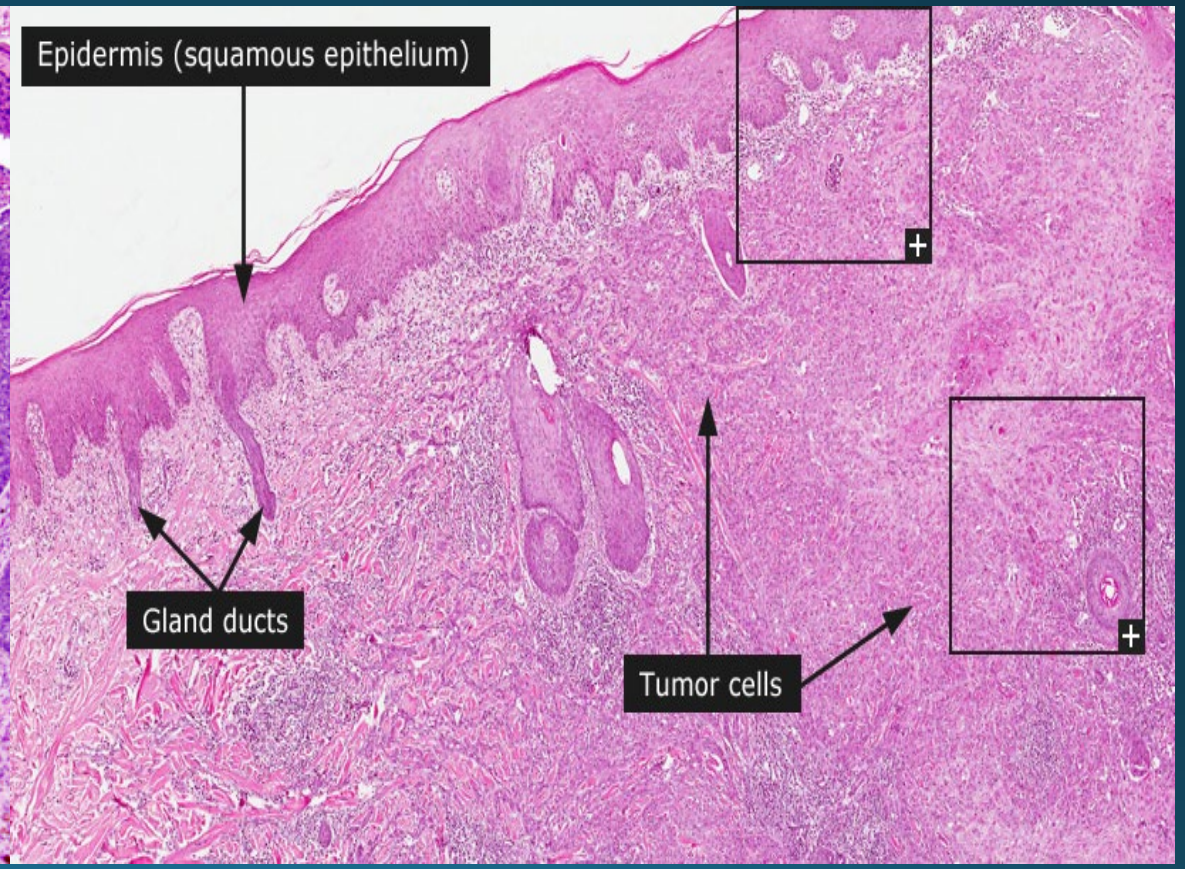
- Squamous-cell carcinoma
- Basal cell carcinoma
- Merkell cell cancer

# Epidemiology

- Most common cancers.
- Risk factors include chronic sun exposure, advanced age, skin that is sensitive to UV radiation, and immunosuppression.
- More than 95% of patients are cured with surgery.
- Locally advanced disease can result in extensive morbidity through tissue destruction.
- Metastatic disease is considered incurable.

# Histopathology





# Characteristics and biologic behavior

- Tumor mutation burden is high because of chronic skin damage from UV light.
- Immune system surveillance is critical for preventing cancer in the immunocompetent.
- Patients who have a primary immuno-compromised system or those on immune-suppressive treatments are up 250 times more likely to get these cancers.

# Cemiplimab in advanced cutaneous SCC

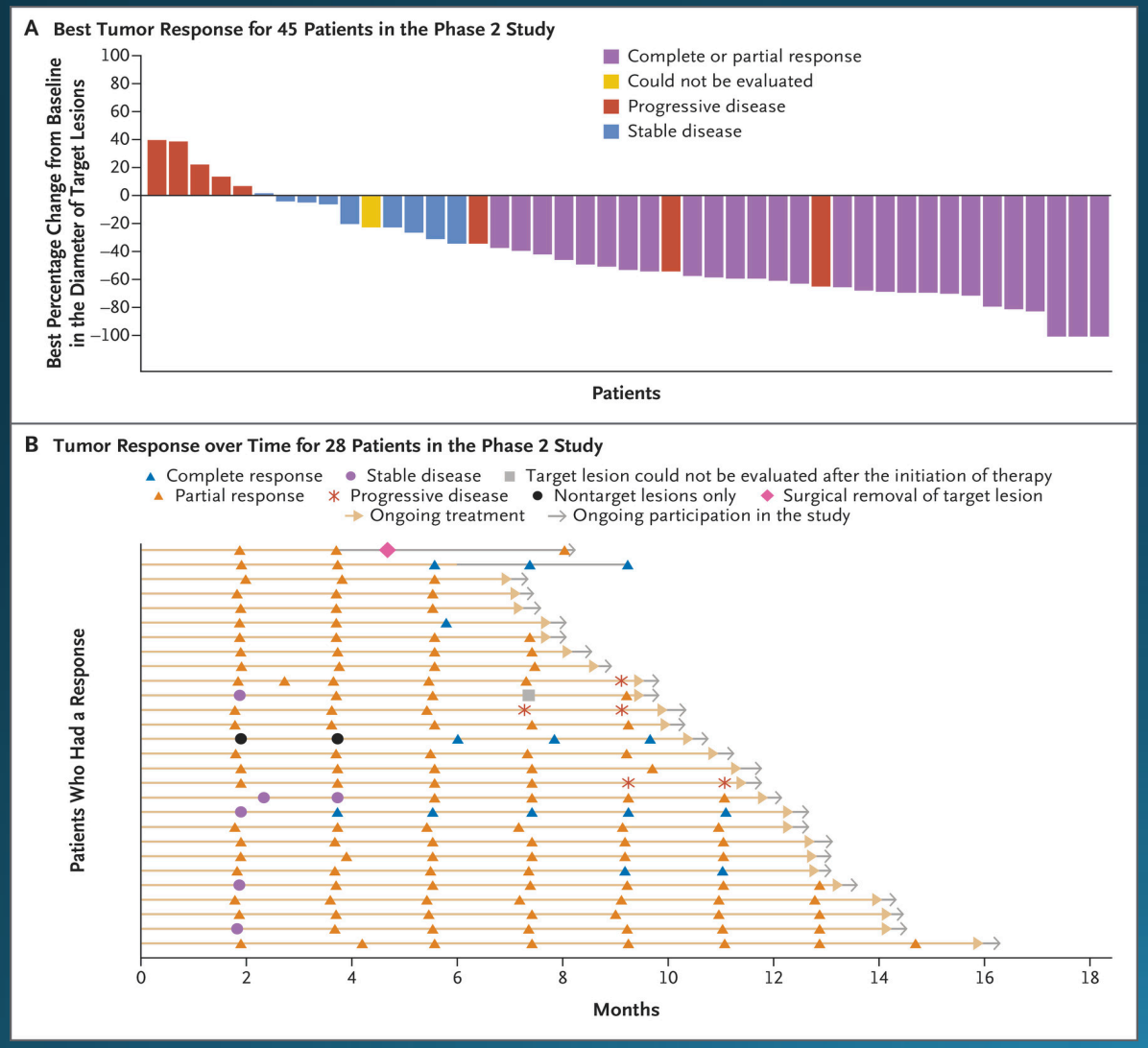
- 75 patients with locally advanced or metastatic cutaneous SCC.

- Cemiplimab 3mg/kg i.v. every 2 weeks.

*RR: 50%
*mTTR: 2.3mths
*DOR: 54% >6mths

NEJM 2018; 379: 341-351

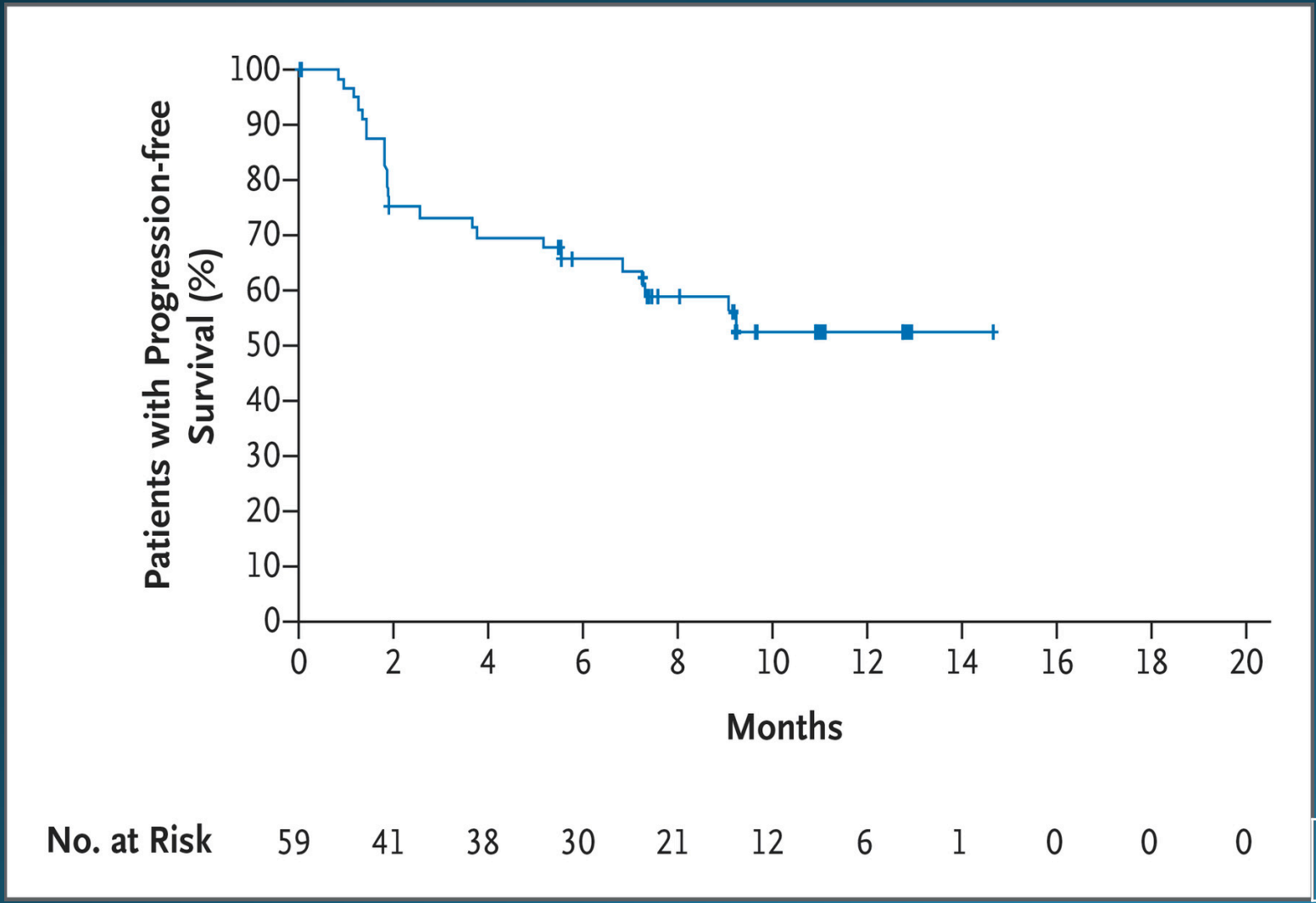
# Cemiplimab in advanced cutaneous SCC




*23-28 (82%) patients who responded continued to respond at the time of data cutoff.

NEJM 2018; 379: 341-351

# Cemiplimab in advanced cutaneous SCC




*PFS 53% at 12 months.
*OS 81% at 12 months.

NEJM 2018; 379: 341-351

# Pembrolizumab in advanced cutaneous SCC

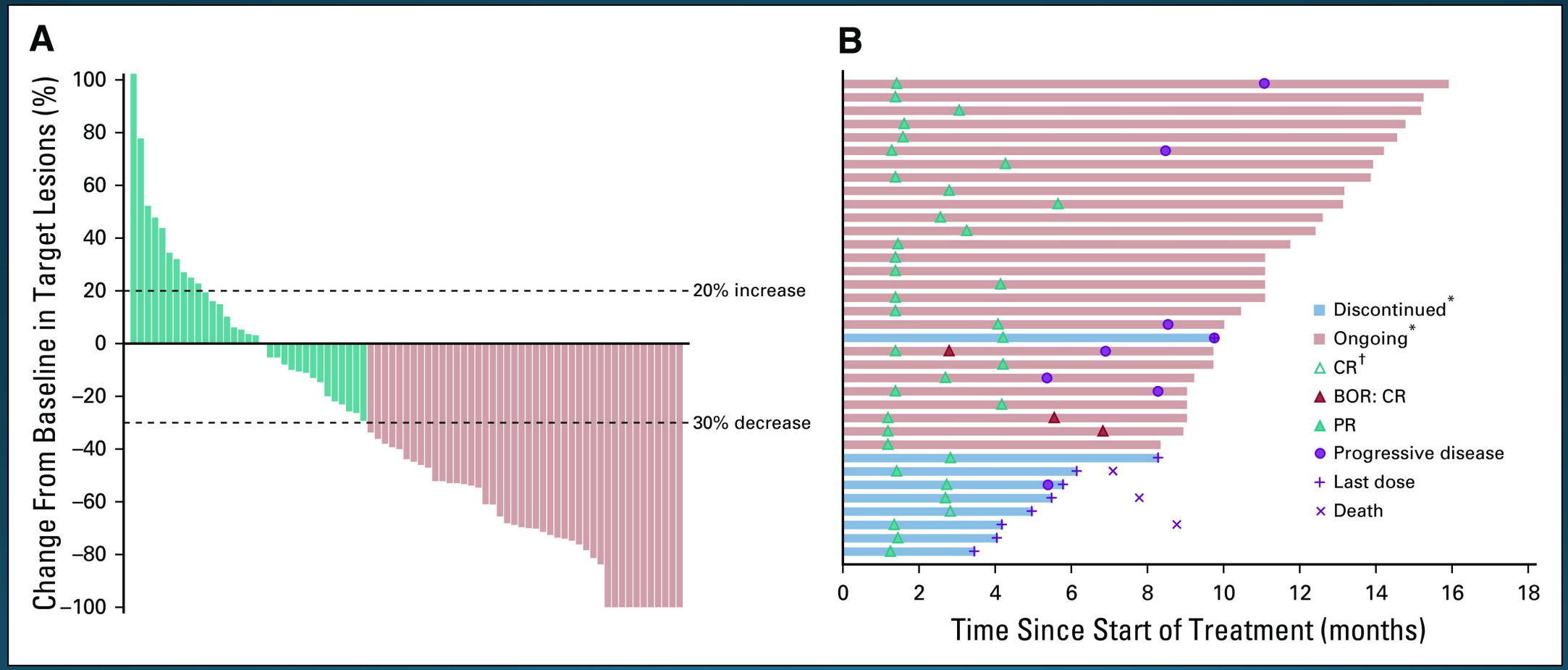
- 105 patients with locally advanced or metastatic cutaneous SCC.

- Pembrolizumab 200mg i.v. every 3 weeks.

*RR: 34%
*mTTR: 1.5mths

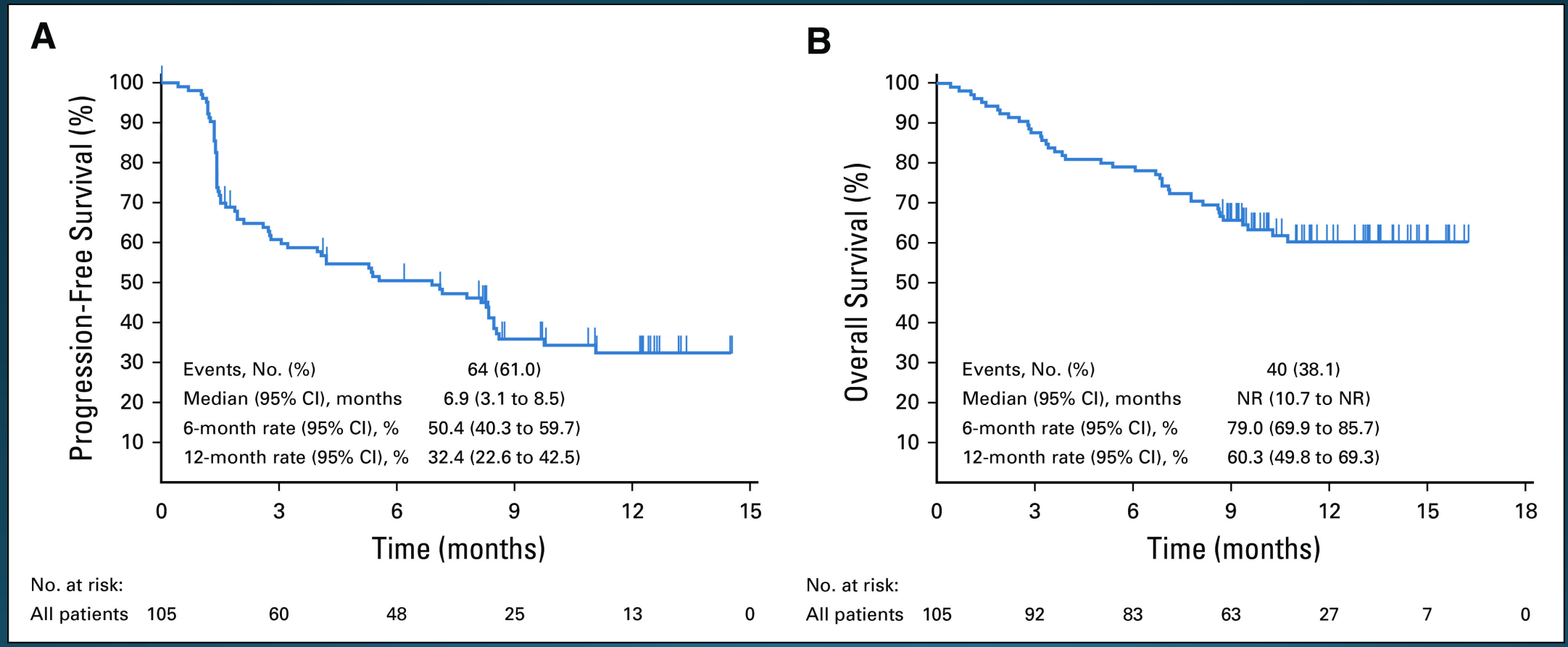
JCO 2020; 25: 2916-2925.

# Pembrolizumab in advanced cutaneous SCC




JCO 2020; 25: 2916-2925.

# Pembrolizumab in advanced cutaneous SCC



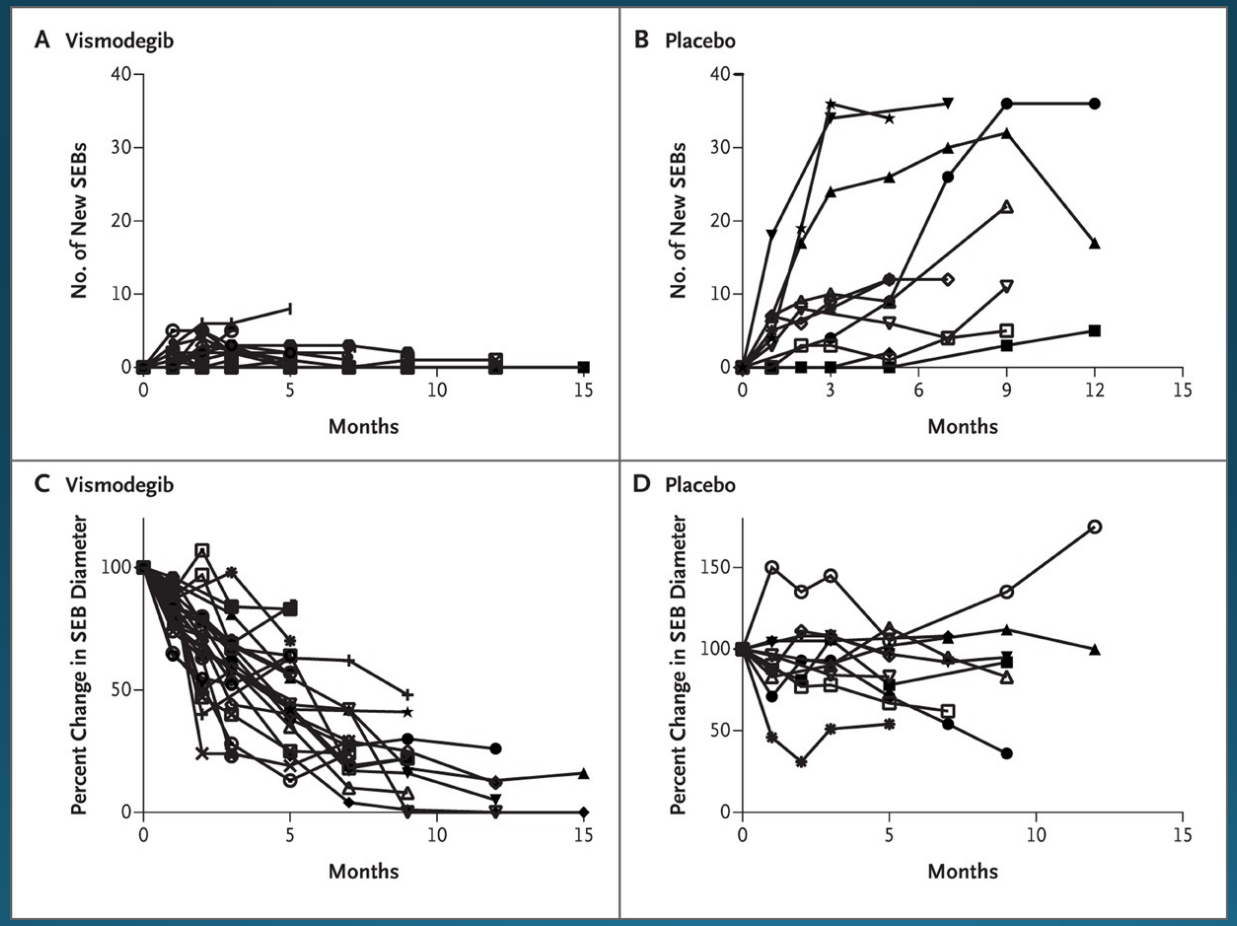

JCO 2020; 25: 2916-2925.

# Vismodegib for basal-cell nevus syndrome

Basal-cell nevus syndrome patients inherit a defective patched 1 (PTCH1) gene. Inhibits the hedgehog signaling pathway.

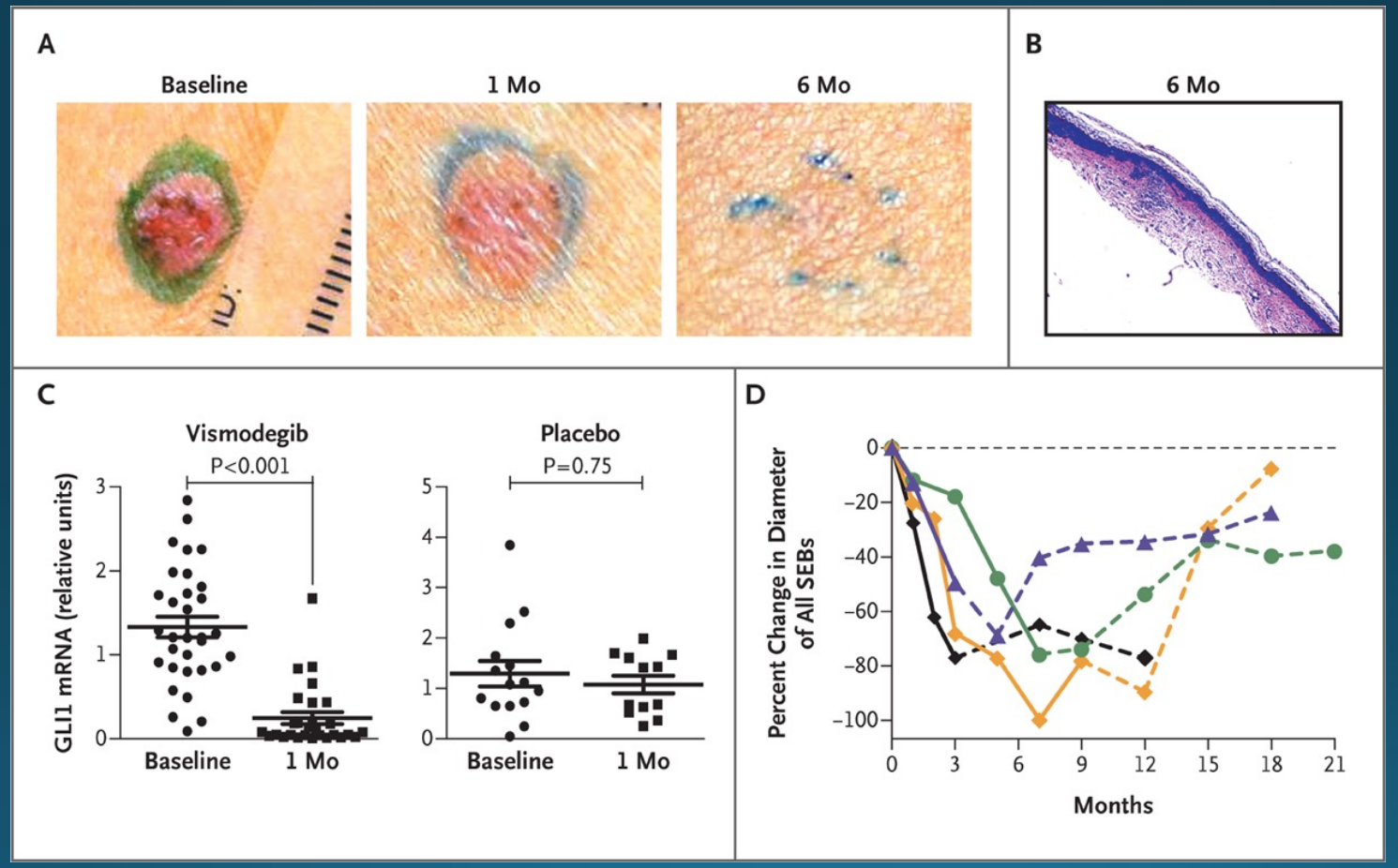
Vismodegib inhibits the hedgehog pathway.

# Vismodegib for basal-cell nevus syndrome




NEJM 2012; 366: 2181-2188.

# Vismodegib for basal nevus syndrome

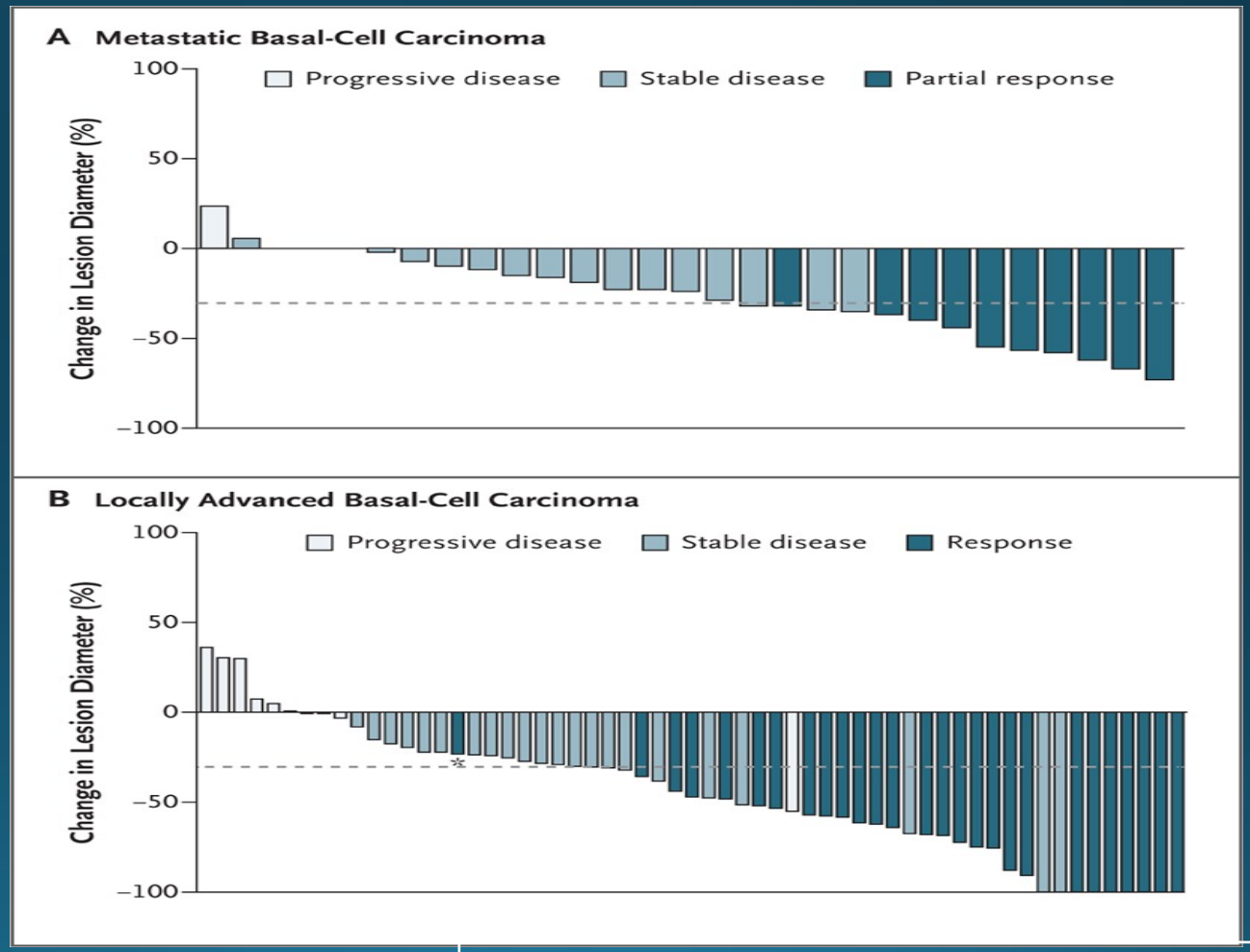



NEJM 2012; 366: 2181-2188.

# Vismodegib for basal-cell carcinoma

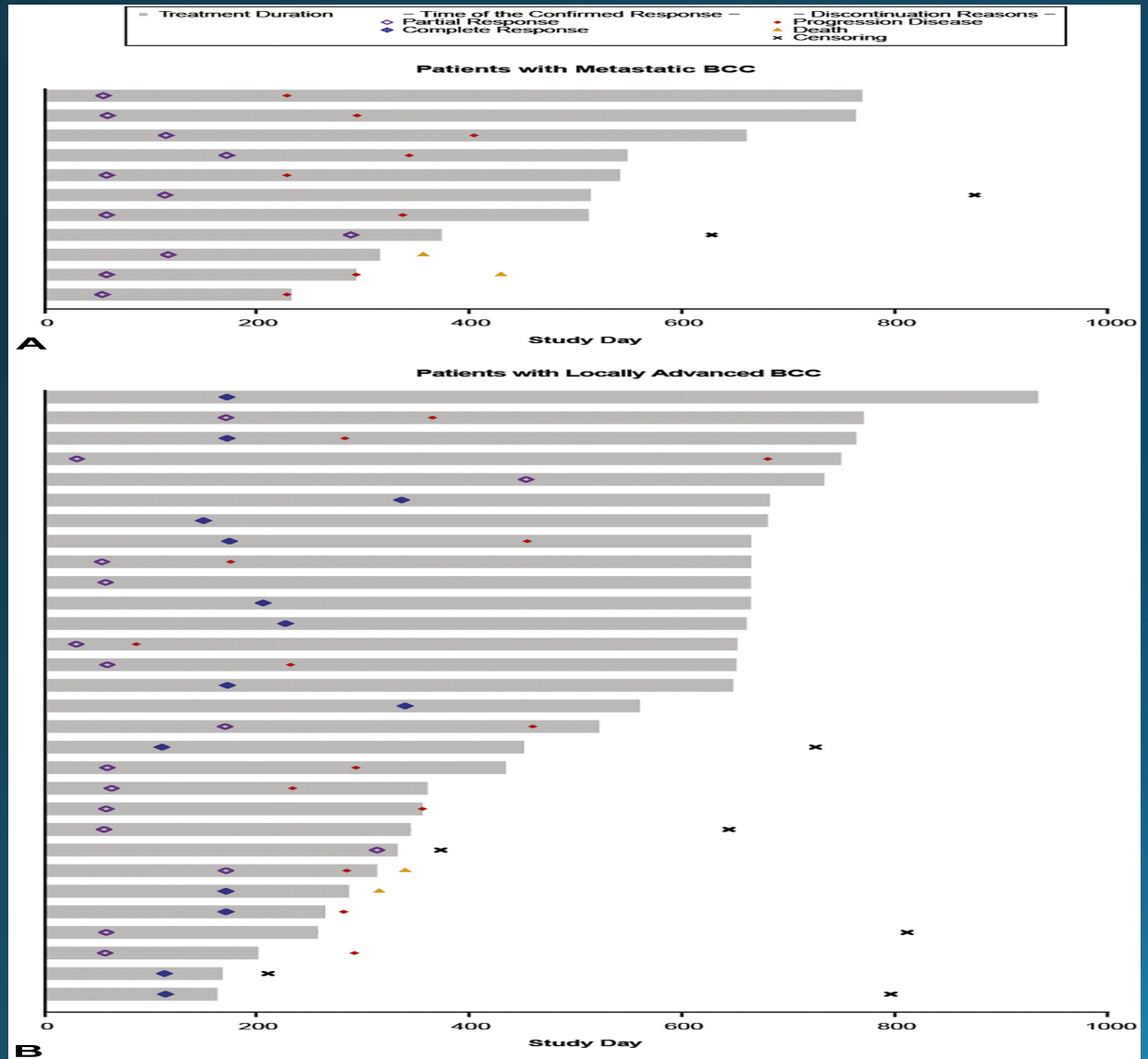
- 99 pts with locally advanced or metastatic disease.

Vismodegib 150mg P.O daily.




NEJM 2012; 366: 2171-2179.

# Vismodegib for basal-cell carcinoma



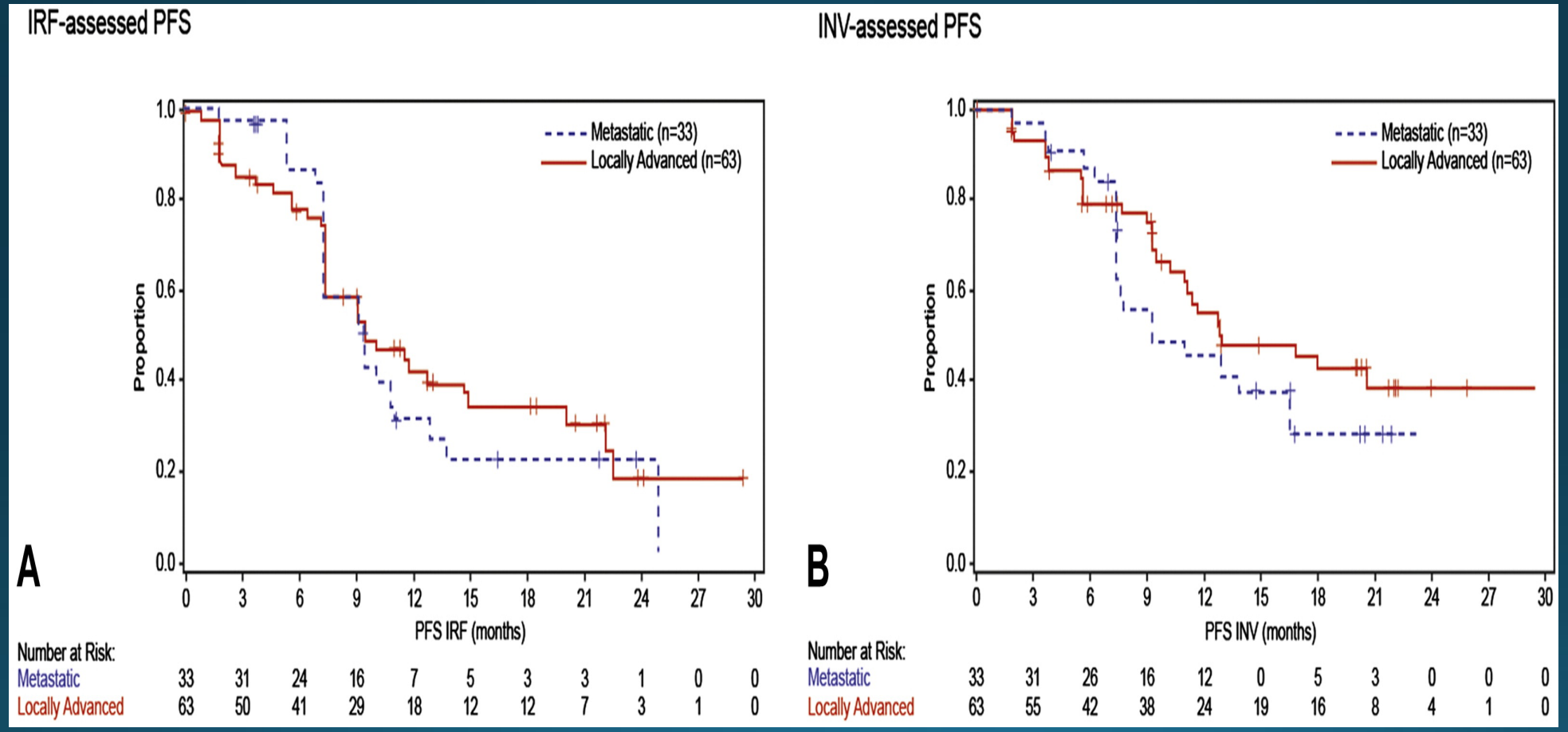

*RR: 33%

*DOR: 9.5mths

*RR: 47%

JAAD 2015; 72: 1021-1026.

# Vismodegib for basal-cell carcinoma




JAAD 2015; 72: 1021-1026.

# Sonidegib for basal-cell carcinoma

- BOLT trial

230 patients with locally advanced or metastatic cutaneous BCC.

- 1:2 randomization

Sonidegib 200mg P.O. daily

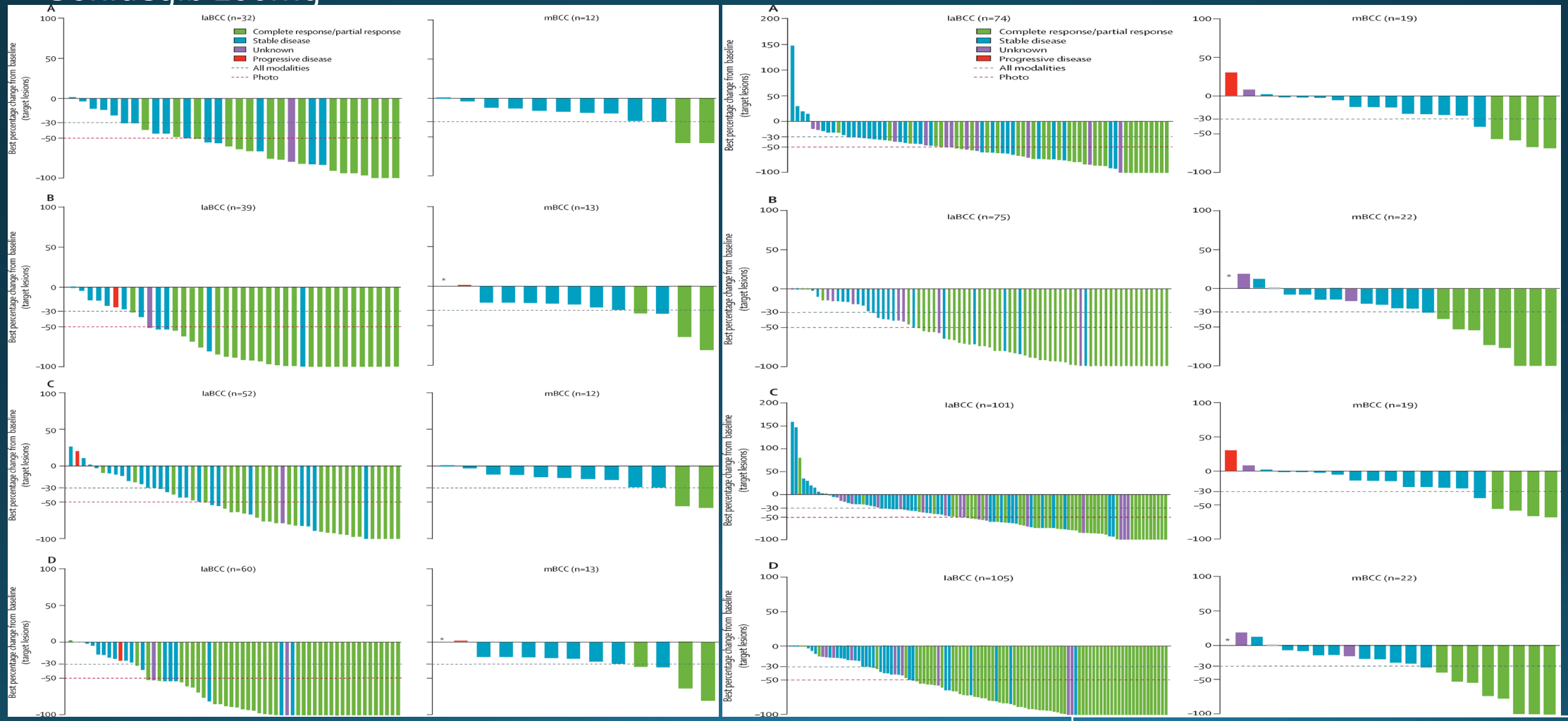
Sonidegib 800mg P.O. daily

Lancet Oncol 2015; 16: 716-728.

# Sonidegib for basal-cell carcinoma

Sonidegib 200mg

Sonidegib 800mg

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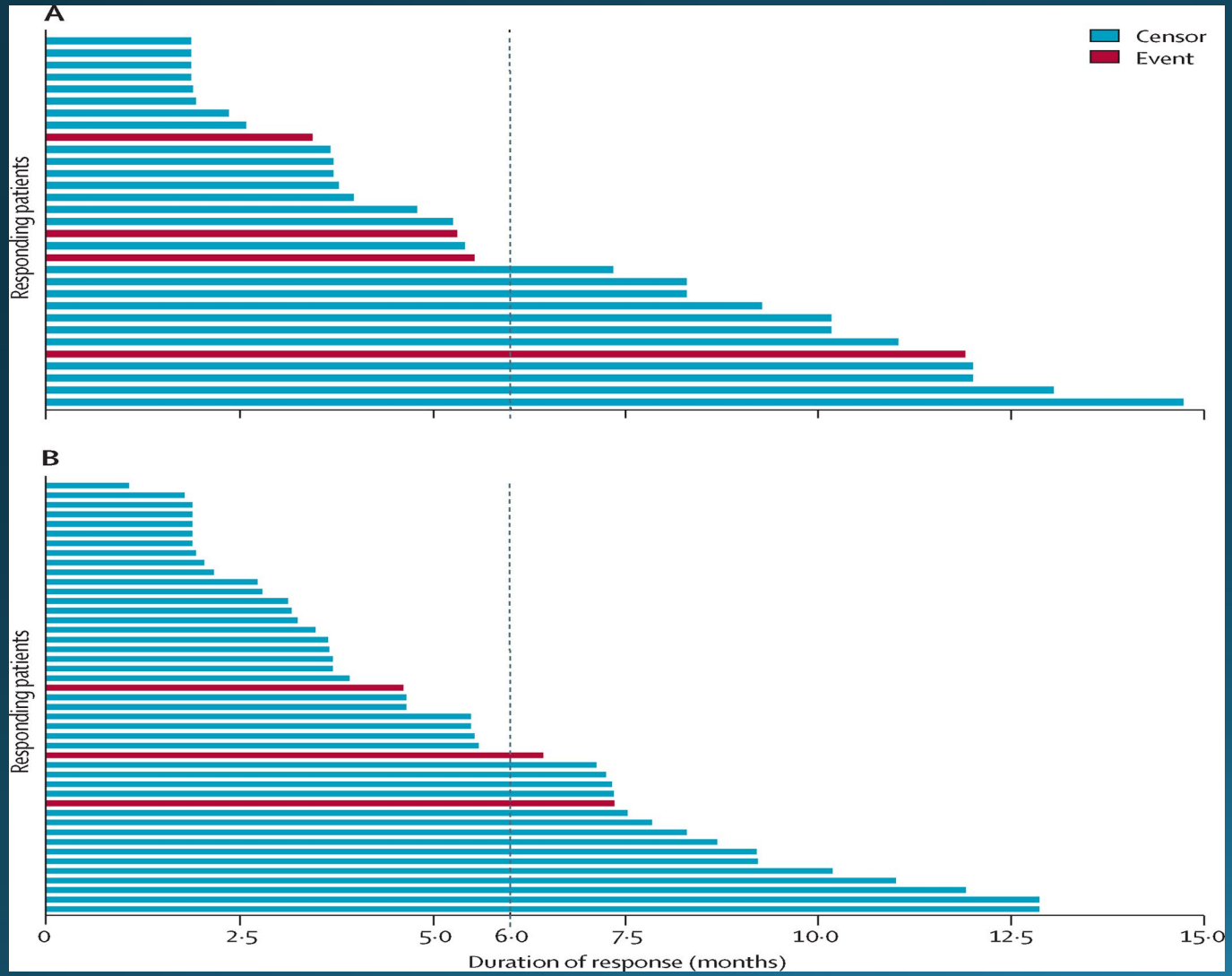
# Sonidegib for basal-cell carcinoma




| | 200mg | 800mg |
|---|---|---|
| • ORR: | 58% | 55% |
| • Dx. Red: | 32% | 60% |
| • Tx. Disc: | 22% | 33% |
| • Gd 3-4 AE: | 14% | 30% |

Lancet Oncol 2015; 16: 716-728.

# Cemiplimab for BCC after progression to HHIS.

- 28 patients with locally advanced or metastatic BCC after progression or intolerance to HHIS.

Cemiplimab 350MG i.v. every 3 weeks.

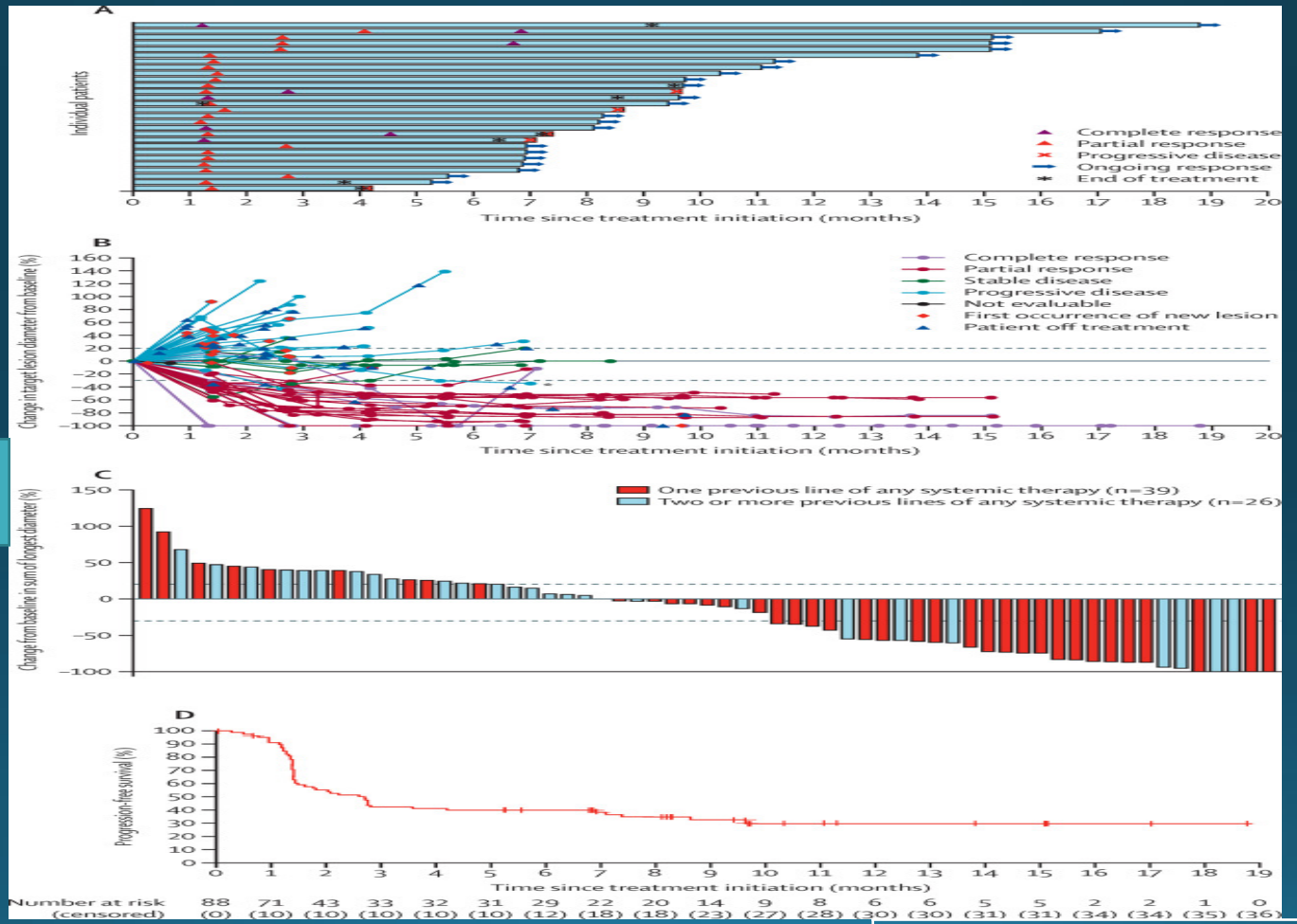
*RR: 28.6%
*mTTR: 3.2 months
*DOR: 9-23 months
*PFS: 8.3 months
*OS: 25.7 months

J Immunother Cancer 2020;8(Suppl3): A428.

# Avelumab for chemotherapy refractory Merkel cell carcinoma.

- 88 pts with chemotx refractory disease.

- Avelumab 10mg/kg i.v. q 2 wks.

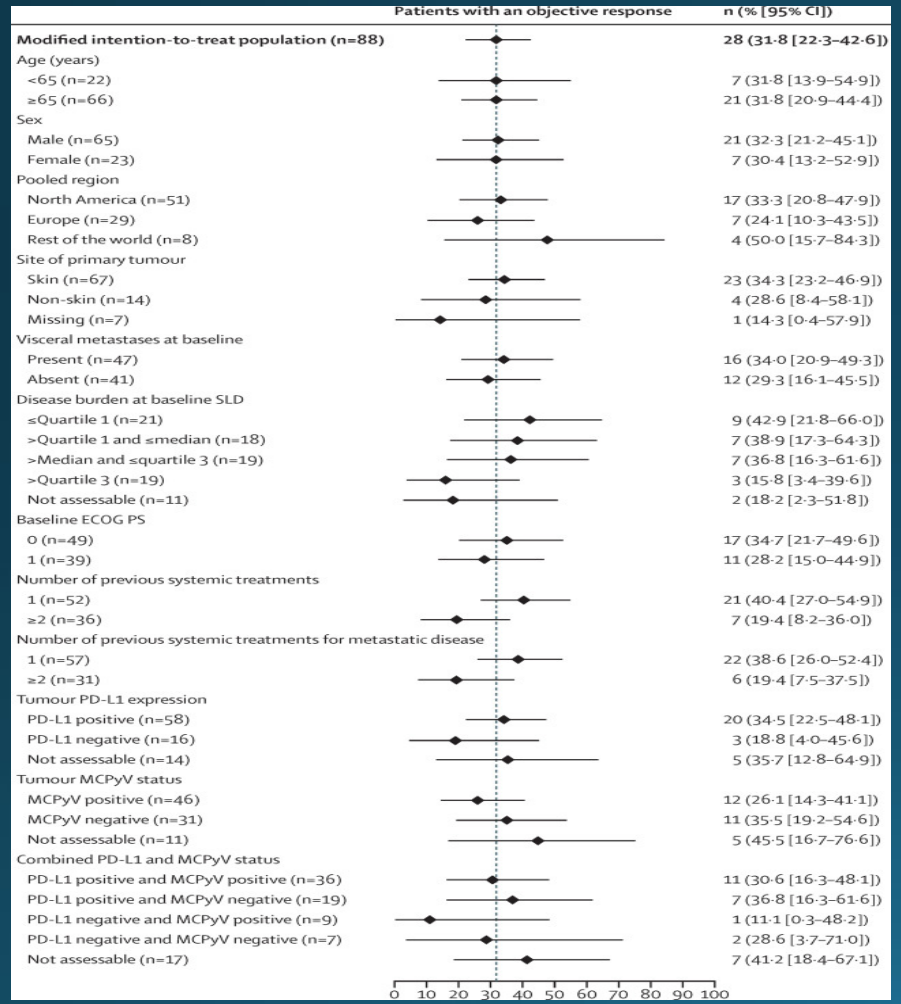



- ORR 28pts
- CR 8 pts
- PR 20 pts
- SD 9 pts

- PFS 2.7 months
- OS 11.3 months

Lancet Oncol 2016; 17: 1374-1385.

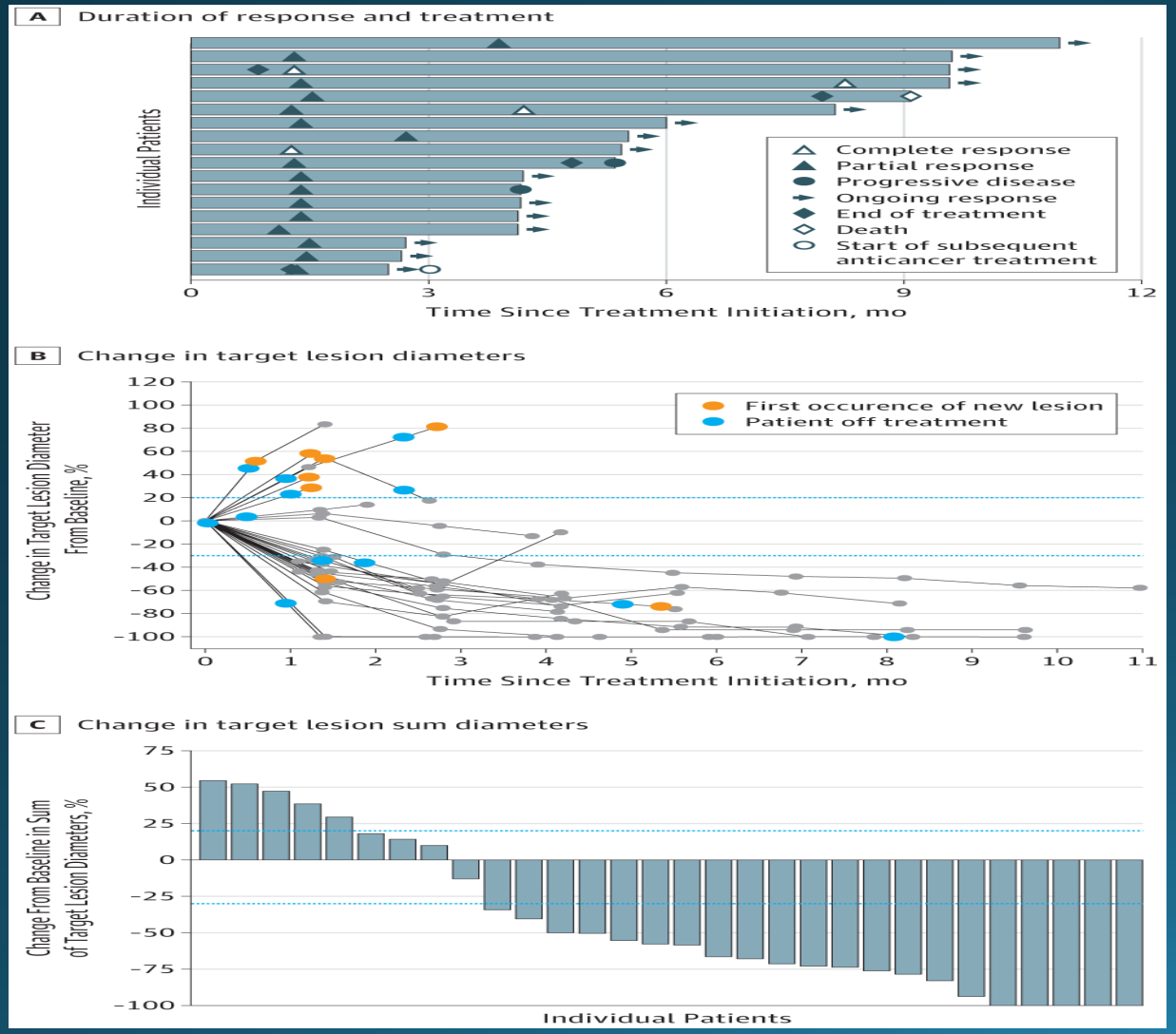
# Avelumab for chemotherapy refractory Merkel cell carcinoma.




Responses were irrespective of PD-L1 expression or Merkel cell polyomavirus status.

Lancet Oncol 2016; 17: 1374-1385.

# Avelumab for chemotherapy refractory Merkel cell carcinoma.



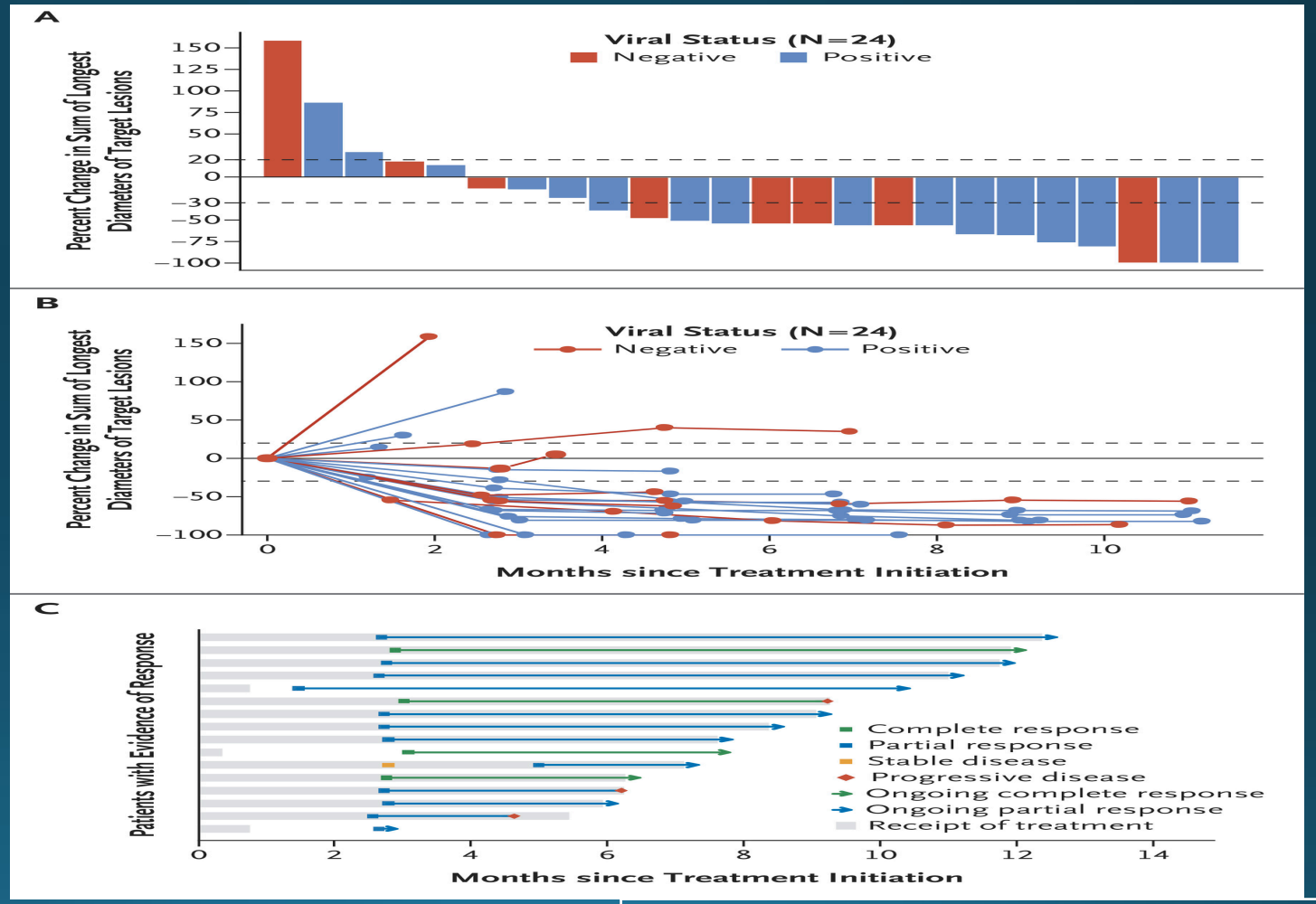

- PFS at 6 months: 40%
- OS at 6 months: 69%

Lancet Oncol 2016; 17: 1374-1385.

# Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.

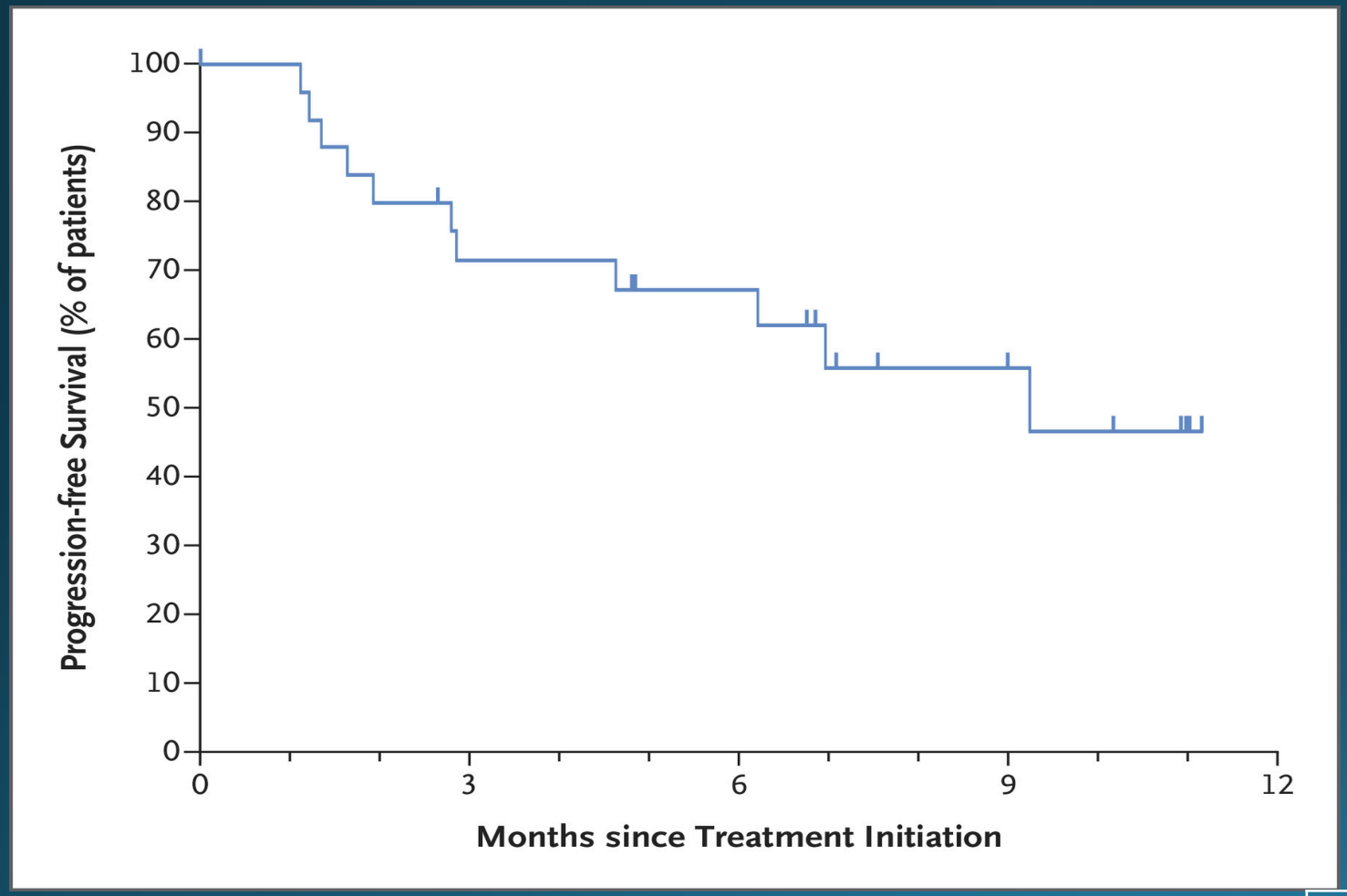
- 26 pts with chemotx naïve MCC.

Pembrolizumab 2mg/kg i.v. q 3 wks.




NEJM 2016; 374: 2542-2552.

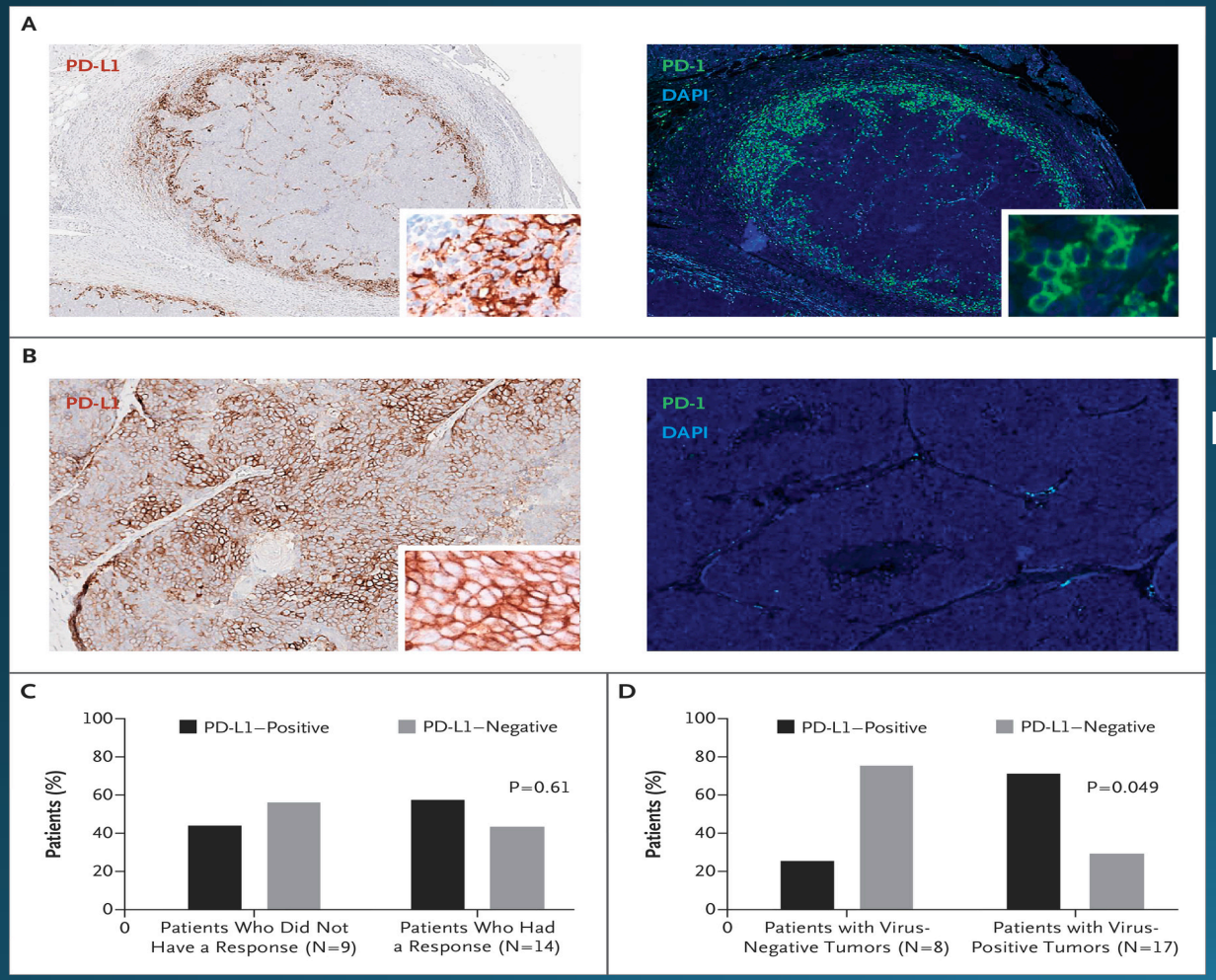
# Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.




- ORR 56%
- CR 4 pts
- PR 10 pts
- SD 1 pt

NEJM 2016; 374: 2542-2552.

# Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.




Responses were irrespective of PD-L1 expression or Merkel cell polyomavirus status.

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